

## SEQUENCE LISTING

<110> Merck & Co., Inc.  
Istituto di Ricerche di Biologia Molecolare P. Angeletti S.p.A.

<120> HCV REPLICONS CONTAINING NS5B FROM  
GENOTYPE 2B

<130> 21564Y PCT

<150> 60/517,605

<151> 2003-11-05

<160> 28

<170> FastSEQ for Windows Version 4.0

<210> 1

<211> 591

<212> PRT

<213> Artificial Sequence

<220>

<223> modified NS5B

<221> VARIANT

<222> (5)...(5)

<223> Xaa = threonine or serine

<221> VARIANT

<222> (24)...(24)

<223> Xaa = asparagine or serine

<221> VARIANT

<222> (31)...(31)

<223> Xaa = methionine or isoleucine

<221> VARIANT

<222> (376)...(376)

<223> Xaa = isoleucine or leucine

<400> 1

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Phe	His	Asn	Lys	Val	Tyr	Ser	Thr	Thr	Ser	Arg	Ser	Ala	Ser	Leu	Arg
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Ala	Lys	Lys	Val	Thr	Phe	Asp	Arg	Val	Gln	Val	Leu	Asp	Ala	His	Tyr
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Asp	Ser	Val	Leu	Gln	Asp	Val	Lys	Arg	Ala	Ala	Ser	Lys	Val	Ser	Ala
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Arg	Leu	Leu	Thr	Val	Glu	Glu	Ala	Cys	Ala	Leu	Thr	Pro	Pro	His	Ser
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Ala	Lys	Ser	Arg	Tyr	Gly	Phe	Gly	Ala	Lys	Glu	Val	Arg	Ser	Leu	Ser
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	130					135					140				
Phe	Cys	Ile	Asp	Pro	Thr	Lys	Gly	Gly	Lys	Lys	Pro	Ala	Arg	Leu	Ile
145					150					155					160
Val	Tyr	Pro	Asp	Leu	Gly	Val	Arg	Val	Cys	Glu	Lys	Met	Ala	Leu	Tyr
				165					170						175
Asp	Ile	Ala	Gln	Lys	Leu	Pro	Lys	Ala	Ile	Met	Gly	Pro	Ser	Tyr	Gly
			180					185					190		
Phe	Gln	Tyr	Ser	Pro	Ala	Glu	Arg	Val	Asp	Phe	Leu	Leu	Lys	Ala	Trp
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Gly	Ser	Lys	Lys	Asp	Pro	Met	Gly	Phe	Ser	Tyr	Asp	Thr	Arg	Cys	Phe
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Asp	Ser	Thr	Val	Thr	Glu	Arg	Asp	Ile	Arg	Thr	Glu	Glu	Ser	Ile	Tyr
225					230					235					240
Gln	Ala	Cys	Ser	Leu	Pro	Gln	Glu	Ala	Arg	Thr	Val	Ile	His	Ser	Leu
				245					250					255	
Thr	Glu	Arg	Leu	Tyr	Val	Gly	Gly	Pro	Met	Thr	Asn	Ser	Lys	Gly	Gln
			260					265					270		
Ser	Cys	Gly	Tyr	Arg	Arg	Cys	Arg	Ala	Ser	Gly	Val	Phe	Thr	Thr	Ser
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Met	Gly	Asn	Thr	Met	Thr	Cys	Tyr	Ile	Lys	Ala	Leu	Ala	Ala	Cys	Lys
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Ala	Ala	Gly	Ile	Val	Asp	Pro	Val	Met	Leu	Val	Cys	Gly	Asp	Asp	Leu
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Val	Val	Ile	Ser	Glu	Ser	Gln	Gly	Asn	Glu	Glu	Asp	Glu	Arg	Asn	Leu
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Arg	Ala	Phe	Thr	Glu	Ala	Met	Thr	Arg	Tyr	Ser	Ala	Pro	Pro	Gly	Asp
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Leu	Pro	Arg	Pro	Glu	Tyr	Asp	Leu	Glu	Leu	Ile	Thr	Ser	Cys	Ser	Ser
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Asn	Val	Ser	Val	Ala	Leu	Asp	Ser	Arg	Gly	Arg	Arg	Arg	Tyr	Phe	Leu
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Thr	Arg	Asp	Pro	Thr	Thr	Pro	Xaa	Thr	Arg	Ala	Ala	Trp	Glu	Thr	Val
385					390					395					400
Arg	His	Ser	Pro	Val	Asn	Ser	Trp	Leu	Gly	Asn	Ile	Ile	Gln	Tyr	Ala
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Pro	Thr	Ile	Trp	Val	Arg	Met	Val	Ile	Met	Thr	His	Phe	Phe	Ser	Ile
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Leu	Leu	Ala	Gln	Asp	Thr	Leu	Asn	Gln	Asn	Leu	Asn	Phe	Glu	Met	Tyr
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Glu	Leu	Ser	Arg	Val	Ala	Ala	Thr	Leu	Arg	Lys	Leu	Gly	Ala	Pro	Pro
				485					490					495	
Leu	Arg	Ala	Trp	Lys	Ser	Arg	Ala	Arg	Ala	Val	Arg	Ala	Ser	Leu	Ile
		500						505					510		
Ala	Gln	Gly	Ala	Arg	Ala	Ala	Ile	Cys	Gly	Arg	Tyr	Leu	Phe	Asn	Trp
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Ala	Val	Lys	Thr	Lys	Leu	Lys	Leu	Thr	Pro	Leu	Pro	Glu	Ala	Ser	Arg
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Leu	Asp	Leu	Ser	Gly	Trp	Phe	Thr	Val	Gly	Ala	Gly	Gly	Gly	Asp	Ile
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Tyr	His	Ser	Val	Ser	His	Ala	Arg	Pro	Arg	Leu	Leu	Leu	Leu	Cys	Leu
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 <212> DNA  
 <213> Artificial Sequence

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 <223> modified NS5B

<221> variation  
 <222> (3)...(3)  
 <223> n = A or T

<221> variation  
 <222> (9)...(9)  
 <223> n = C or A

<221> variation  
 <222> (13)...(13)  
 <223> n = A or T

<221> variation  
 <222> (15)...(15)  
 <223> n = A or C

<221> variation  
 <222> (21)...(21)  
 <223> n = A or G

<221> variation  
 <222> (24)...(24)  
 <223> n = C or G

<221> variation  
 <222> (28)...(28)  
 <223> n = T or C

<221> modified\_base  
 <222> (30)...(30)  
 <223> n = G or C

<221> variation  
 <222> (33)...(33)  
 <223> n = C or A

<221> variation  
 <222> (71)...(71)

<223> n = A or G

<221> variation

<222> (83)...(83)

<223> n = G or T

<221> variation

<222> (1174)...(1174)

<223> n = A or C

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acctcgagga	gtgcctctct	gagggcaaag	aaggtgactt	ttgacagggt	gcaggtgctg	180
gacgcacact	atgactcagt	cttgcaggac	gttaagcggg	ccgcctctaa	ggttagtgcg	240
aggctcctca	cggtagagga	agcctgcgcg	ctgaccccg	cccactccgc	caaatcgcg	300
tacggatttg	gggcaaaaga	ggtgcgcagc	ttatctagga	gggccgttaa	ccacatccgg	360
tccgtgtggg	aggacctcct	ggaagaccaa	cataccccaa	ttgacacaa	tatcatggct	420
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gtcgatttcc	tcctcaaagc	ttgggggaag	aagaaggacc	caatgggggt	ctcgatgac	660
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gagcttataa	catcctgctc	ctcaaacgta	tcggtagcgc	tggactctcg	gggtcgccgc	1140
cgggtacttcc	taaccagaga	ccctaccact	ccantcacc	gagctgcttg	ggaaacagta	1200
agacactccc	ctgtcaattc	ttggctgggc	aacatcatcc	agtacgcccc	cacaatctgg	1260
gtccggatgg	tcataatgac	tcacttcttc	tccatactat	tggcccagga	cactctgaac	1320
caaaatctca	attttgagat	gtacggggca	gtatactcgg	tcaatccatt	agacctaccg	1380
gccataattg	aaaggctaca	tgggcttgaa	gccttttcac	tgcacacata	ctctccccac	1440
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aagagtcggg	cgcgtgccgt	gagagcttca	ctcatcgccc	aaggagcgag	ggcggccatt	1560
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<210> 3

<211> 1394

<212> PRT

<213> Artificial Sequence

<220>

<223> modified NS3-5A

<221> VARIANT

<222> (1215)...(1215)

<223> Xaa = asparagine or serine

<221> VARIANT

&lt;222&gt; (904)...(904)

&lt;223&gt; Xaa = valine or alanine

&lt;400&gt; 3

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			20					25					30		
Glu	Val	Gln	Val	Val	Ser	Thr	Ala	Thr	Gln	Ser	Phe	Leu	Ala	Thr	Cys
		35					40					45			
Val	Asn	Gly	Val	Cys	Trp	Thr	Val	Tyr	His	Gly	Ala	Gly	Ser	Lys	Thr
	50					55					60				
Leu	Ala	Gly	Pro	Lys	Gly	Pro	Ile	Thr	Gln	Met	Tyr	Thr	Asn	Val	Asp
65					70					75					80
Gln	Asp	Leu	Val	Gly	Trp	Gln	Ala	Pro	Pro	Gly	Ala	Arg	Ser	Leu	Thr
				85					90					95	
Pro	Cys	Thr	Cys	Gly	Ser	Ser	Asp	Leu	Tyr	Leu	Val	Thr	Arg	His	Ala
			100					105					110		
Asp	Val	Ile	Pro	Val	Arg	Arg	Arg	Gly	Asp	Ser	Arg	Gly	Ser	Leu	Leu
		115					120					125			
Ser	Pro	Arg	Pro	Val	Ser	Tyr	Leu	Lys	Gly	Ser	Ser	Gly	Gly	Pro	Leu
	130					135					140				
Leu	Cys	Pro	Ser	Gly	His	Ala	Val	Gly	Ile	Phe	Arg	Ala	Ala	Val	Cys
145					150					155					160
Thr	Arg	Gly	Val	Ala	Lys	Ala	Val	Asp	Phe	Val	Pro	Val	Glu	Ser	Met
				165					170					175	
Glu	Thr	Thr	Met	Arg	Ser	Pro	Val	Phe	Thr	Asp	Asn	Ser	Ser	Pro	Pro
			180					185					190		
Ala	Val	Pro	Gln	Thr	Phe	Gln	Val	Ala	His	Leu	His	Ala	Pro	Thr	Gly
		195					200					205			
Ser	Gly	Lys	Ser	Thr	Lys	Val	Pro	Ala	Ala	Tyr	Ala	Ala	Gln	Gly	Tyr
	210					215					220				
Lys	Val	Leu	Val	Leu	Asn	Pro	Ser	Val	Ala	Ala	Thr	Leu	Gly	Phe	Gly
225					230					235					240
Ala	Tyr	Met	Ser	Lys	Ala	His	Gly	Ile	Asp	Pro	Asn	Ile	Arg	Thr	Gly
				245					250					255	
Val	Arg	Thr	Ile	Thr	Thr	Gly	Ala	Pro	Val	Thr	Tyr	Ser	Thr	Tyr	Gly
			260					265					270		
Lys	Phe	Leu	Ala	Asp	Gly	Gly	Cys	Ser	Gly	Gly	Ala	Tyr	Asp	Ile	Ile
		275					280					285			
Ile	Cys	Asp	Glu	Cys	His	Ser	Thr	Asp	Ser	Thr	Thr	Ile	Leu	Gly	Ile
	290					295					300				
Gly	Thr	Val	Leu	Asp	Gln	Ala	Glu	Thr	Ala	Gly	Ala	Arg	Leu	Val	Val
305					310					315					320
Leu	Ala	Thr	Ala	Thr	Pro	Pro	Gly	Ser	Val	Thr	Val	Pro	His	Pro	Asn
				325					330					335	
Ile	Glu	Glu	Val	Ala	Leu	Ser	Asn	Thr	Gly	Glu	Ile	Pro	Phe	Tyr	Gly
			340					345					350		
Lys	Ala	Ile	Pro	Ile	Glu	Ala	Ile	Arg	Gly	Gly	Arg	His	Leu	Ile	Phe
		355					360					365			
Cys	His	Ser	Lys	Lys	Lys	Cys	Asp	Glu	Leu	Ala	Ala	Lys	Leu	Ser	Gly
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Leu	Gly	Ile	Asn	Ala	Val	Ala	Tyr	Tyr	Arg	Gly	Leu	Asp	Val	Ser	Val
385					390					395					400

Ile	Pro	Thr	Ile	Gly	Asp	Val	Val	Val	Val	Ala	Thr	Asp	Ala	Leu	Met
				405					410					415	
Thr	Gly	Tyr	Thr	Gly	Asp	Phe	Asp	Ser	Val	Ile	Asp	Cys	Asn	Thr	Cys
			420				425						430		
Val	Thr	Gln	Thr	Val	Asp	Phe	Ser	Leu	Asp	Pro	Thr	Phe	Thr	Ile	Glu
		435					440					445			
Thr	Thr	Thr	Val	Pro	Gln	Asp	Ala	Val	Ser	Arg	Ser	Gln	Arg	Arg	Gly
	450					455					460				
Arg	Thr	Gly	Arg	Gly	Arg	Met	Gly	Ile	Tyr	Arg	Phe	Val	Thr	Pro	Gly
465					470					475					480
Glu	Arg	Pro	Ser	Gly	Met	Phe	Asp	Ser	Ser	Val	Leu	Cys	Glu	Cys	Tyr
				485					490					495	
Asp	Ala	Gly	Cys	Ala	Trp	Tyr	Glu	Leu	Thr	Pro	Ala	Glu	Thr	Ser	Val
			500					505					510		
Arg	Leu	Arg	Ala	Tyr	Leu	Asn	Thr	Pro	Gly	Leu	Pro	Val	Cys	Gln	Asp
		515					520					525			
His	Leu	Glu	Phe	Trp	Glu	Ser	Val	Phe	Thr	Gly	Leu	Thr	His	Ile	Asp
	530					535					540				
Ala	His	Phe	Leu	Ser	Gln	Thr	Lys	Gln	Ala	Gly	Asp	Asn	Phe	Pro	Tyr
545					550					555					560
Leu	Val	Ala	Tyr	Gln	Ala	Thr	Val	Cys	Ala	Arg	Ala	Gln	Ala	Pro	Pro
				565					570					575	
Pro	Ser	Trp	Asp	Gln	Met	Trp	Lys	Cys	Leu	Ile	Arg	Leu	Lys	Pro	Thr
			580					585					590		
Leu	His	Gly	Pro	Thr	Pro	Leu	Leu	Tyr	Arg	Leu	Gly	Ala	Val	Gln	Asn
		595					600					605			
Glu	Val	Thr	Leu	Thr	His	Pro	Ile	Thr	Lys	Tyr	Ile	Met	Ala	Cys	Met
	610					615					620				
Ser	Ala	Asp	Leu	Glu	Val	Val	Thr	Ser	Thr	Trp	Val	Leu	Val	Gly	Gly
625					630					635					640
Val	Leu	Ala	Ala	Leu	Ala	Ala	Tyr	Cys	Leu	Thr	Thr	Gly	Ser	Val	Val
				645					650					655	
Ile	Val	Gly	Arg	Ile	Ile	Leu	Ser	Gly	Arg	Pro	Ala	Ile	Val	Pro	Asp
			660					665					670		
Arg	Glu	Phe	Leu	Tyr	Gln	Glu	Phe	Asp	Glu	Met	Glu	Glu	Cys	Ala	Ser
		675					680					685			
His	Leu	Pro	Tyr	Ile	Glu	Gln	Gly	Met	Gln	Leu	Ala	Glu	Gln	Phe	Lys
	690					695					700				
Gln	Lys	Ala	Leu	Gly	Leu	Leu	Gln	Thr	Ala	Thr	Lys	Gln	Ala	Glu	Ala
705					710					715					720
Ala	Ala	Pro	Val	Val	Glu	Ser	Lys	Trp	Arg	Ala	Leu	Glu	Thr	Phe	Trp
				725					730					735	
Ala	Lys	His	Met	Trp	Asn	Phe	Ile	Ser	Gly	Ile	Gln	Tyr	Leu	Ala	Gly
			740					745					750		
Leu	Ser	Thr	Leu	Pro	Gly	Asn	Pro	Ala	Ile	Ala	Ser	Leu	Met	Ala	Phe
		755					760					765			
Thr	Ala	Ser	Ile	Thr	Ser	Pro	Leu	Thr	Thr	Gln	Ser	Thr	Leu	Leu	Phe
	770					775					780				
Asn	Ile	Leu	Gly	Gly	Trp	Val	Ala	Ala	Gln	Leu	Ala	Pro	Pro	Ser	Ala
785					790					795					800
Ala	Ser	Ala	Phe	Val	Gly	Ala	Gly	Ile	Ala	Gly	Ala	Ala	Val	Gly	Ser
				805					810					815	
Ile	Gly	Leu	Gly	Lys	Val	Leu	Val	Asp	Ile	Leu	Ala	Gly	Tyr	Gly	Ala
			820					825					830		



Gly	Val	Ala	Gly	Ala	Leu	Val	Ala	Phe	Lys	Val	Met	Ser	Gly	Glu	Met
		835					840					845			
Pro	Ser	Thr	Glu	Asp	Leu	Val	Asn	Leu	Leu	Pro	Ala	Ile	Leu	Ser	Pro
		850					855				860				
Gly	Ala	Leu	Val	Val	Gly	Val	Val	Cys	Ala	Ala	Ile	Leu	Arg	Arg	His
865					870					875					880
Val	Gly	Pro	Gly	Glu	Gly	Ala	Val	Gln	Trp	Met	Asn	Arg	Leu	Ile	Ala
				885					890					895	
Phe	Ala	Ser	Arg	Gly	Asn	His	Xaa	Ser	Pro	Thr	His	Tyr	Val	Pro	Glu
			900					905					910		
Ser	Asp	Ala	Ala	Ala	Arg	Val	Thr	Gln	Ile	Leu	Ser	Ser	Leu	Thr	Ile
		915					920					925			
Thr	Gln	Leu	Leu	Lys	Arg	Leu	His	Gln	Trp	Ile	Asn	Glu	Asp	Cys	Ser
		930				935					940				
Thr	Pro	Cys	Ser	Gly	Ser	Trp	Leu	Arg	Asp	Val	Trp	Asp	Trp	Ile	Cys
945					950					955					960
Thr	Val	Leu	Thr	Asp	Phe	Lys	Thr	Trp	Leu	Gln	Ser	Lys	Leu	Leu	Pro
				965					970					975	
Gln	Leu	Pro	Gly	Val	Pro	Phe	Phe	Ser	Cys	Gln	Arg	Gly	Tyr	Lys	Gly
			980					985					990		
Val	Trp	Arg	Gly	Asp	Gly	Ile	Met	Gln	Thr	Thr	Cys	Pro	Cys	Gly	Ala
		995					1000					1005			
Gln	Ile	Thr	Gly	His	Val	Lys	Asn	Gly	Ser	Met	Arg	Ile	Val	Gly	Pro
		1010				1015					1020				
Lys	Thr	Cys	Ser	Asn	Thr	Trp	His	Gly	Thr	Phe	Pro	Ile	Asn	Ala	Tyr
1025					1030					1035					1040
Thr	Thr	Gly	Pro	Cys	Thr	Pro	Ser	Pro	Ala	Pro	Asn	Tyr	Ser	Arg	Ala
				1045					1050					1055	
Leu	Trp	Arg	Val	Ala	Ala	Glu	Glu	Tyr	Val	Glu	Val	Thr	Arg	Val	Gly
			1060					1065					1070		
Asp	Phe	His	Tyr	Val	Thr	Gly	Met	Thr	Thr	Asp	Asn	Val	Lys	Cys	Pro
		1075					1080					1085			
Cys	Gln	Val	Pro	Ala	Pro	Glu	Phe	Phe	Thr	Glu	Val	Asp	Gly	Val	Arg
		1090				1095						1100			
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Thr	Phe	Gln	Val	Gly	Leu	Asn	Gln	Tyr	Leu	Val	Gly	Ser	Gln	Leu	Pro
				1125					1130					1135	
Cys	Glu	Pro	Glu	Pro	Asp	Val	Ala	Val	Leu	Thr	Ser	Met	Leu	Thr	Asp
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Pro	Ser	His	Ile	Thr	Ala	Glu	Thr	Ala	Lys	Arg	Arg	Leu	Ala	Arg	Gly
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Ser	Pro	Pro	Ser	Leu	Ala	Ser	Ser	Ser	Ala	Ile	Gln	Leu	Ser	Ala	Pro
				1170		1175					1180				
Ser	Leu	Lys	Ala	Thr	Cys	Thr	Thr	His	His	Val	Ser	Pro	Asp	Ala	Asp
1185					1190					1195					1200
Leu	Ile	Glu	Ala	Asn	Leu	Leu	Trp	Arg	Gln	Glu	Met	Gly	Gly	Xaa	Ile
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Thr	Arg	Val	Glu	Ser	Glu	Asn	Lys	Val	Val	Val	Leu	Asp	Ser	Phe	Asp
			1220					1225					1230		
Pro	Leu	Arg	Ala	Glu	Glu	Asp	Glu	Arg	Glu	Val	Ser	Val	Pro	Ala	Glu
		1235					1240					1245			
Ile	Leu	Arg	Lys	Ser	Lys	Lys	Phe	Pro	Ala	Ala	Met	Pro	Ile	Trp	Ala
					1250		1255				1260				

Arg Pro Asp Tyr Asn Pro Pro Leu Leu Glu Ser Trp Lys Asp Pro Asp  
 1265 1270 1275 1280  
 Tyr Val Pro Pro Val Val His Gly Cys Pro Leu Pro Pro Ile Lys Ala  
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 Pro Pro Ile Pro Pro Pro Arg Arg Lys Arg Thr Val Val Leu Thr Glu  
 1300 1305 1310  
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